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PRINCIPAL INVESTIGATOR: Susan P. Proctor, D.Sc.
Kristin Jenson Heaton, Ph.D.

CONTRACTING ORGANIZATION: The Henry Jackson Foundation for the Advancement of Military Medicine, Inc.
Rockville, MD 20852

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Kristin J. Heaton, Ph.D. and Susan P. Proctor, D.Sc.

E-Mail: susan.proctor@us.army.mil

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14. ABSTRACT

The ability to accurately and efficiently monitor the neurocognitive status of US warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and network-centered initiatives of the United States military. The Automated Neuropsychological Assessment Metrics (ANAM) is a computer assisted tool for evaluating neurocognitive performance with demonstrated effectiveness for application in diverse military operational and research testing scenarios. The primary objective of this project is to examine select psychometric and administration properties of the newly-released ANAM4. Four studies are proposed that will 1) examine common use practices and determine the effect of specific administration procedures on ANAM4 performance, 2) assess the test-retest reliability of individual ANAM4 tests, 3) examine the validity of the ANAM4 mood scale, and 4) develop a representative normative dataset for Army National Guard service members. Data collection is complete for Studies 1, 2 and 3; data analysis and manuscript preparation is underway for all three studies. Data collection is underway for Study 4.

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ANAM, neurobehavioral, assessment, psychometrics, validity, reliability, normative

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INTRODUCTION

The ability to accurately and efficiently monitor neurocognitive status of U.S. warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and network-centered initiatives of the U.S. military. The Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is a computer-assisted tool for evaluating neurocognitive performance with demonstrated efficacy for application in diverse military operational and research testing scenarios. The primary objective of this multi-study project is to examine select psychometric and administration properties of the ANAM4. This project includes four studies that will i) examine common use practices and determine the effect of specific administration procedures on ANAM4 performance (Study 1), ii) assess the test-retest reliability of individual ANAM4 tests (Study 2), iii) examine the validity of the ANAM4 mood scale (Study 3), and iv) develop a representative normative dataset for Army National Guard Service members (Study 4).

Body

This project was funded 01 December 2007. The approved study timeline/SOW is presented in **Table 1** (with tasks revised as indicated in the approved modification (#12), May 2011).

TABLE 1: STATEMENT OF WORK: *Study Timeline*

Year 1	**Months 1-2**	**Task 1**	Plan and finalize logistics for Phase I (Studies 1-3)
	Months 3-12 (Dec 2008)	**Task 2**	Subject recruitment, data collection and data management for Studies 1-3
Year 2	**Month 13-14**	**Task 3**	Perform preliminary data analyses for Study 3
	Month 15-24 (Dec 2009)	**Task 4**	Complete data collection for Study 1
		Task 5	Perform preliminary data analyses for Study 1
		Task 6	Continue recruitment, data collection and data management for Study 2 & 3
		Task 7	Complete data collection for Study 3
Year 3	**Month 25-36 (Dec 2010)**	**Task 8**	Complete data collection for Study 2
		Task 9	Plan and finalize logistics for Phase II (modified Study 4)
		Task 10	Complete data analyses for Studies 1, 2, 3
		Task 11	Preparation of journal manuscript(s) for Studies 1, 2, 3
		Task 12	Preparation of Project report for Studies 1, 2, 3
		Task 13	Set-up data management procedures for Study 4
Year 4	**Month 37-48 (Dec 2011)**	**Task 14**	Initiate data collection procedures for Study 4
		Task 15	Carry out data collection procedures for Study 4
		Task 16	Initiate integrative data management structure set up for Study 4
		Task 17	Operationalize database for Study 4 analysis scheme
		Task 18	Perform preliminary data analyses for Study 4
		Task 19	Complete data collection procedures for Study 4
Year 5	**Month 49-60 (Dec 2012)**	**Task 20**	Complete data analyses for Study 4
		Task 21	Prepare Study 4 manuscript(s) for peer review
		Task 22	Preparation of Project Final Report

<u>Task 1 (Month 1-2)</u>
Plan and finalize logistics for Phase I (Studies 1-3) – COMPLETED
All logistical aspects for HURC approved studies (Studies 1-3) have been confirmed. Recruitment procedures, equipment, testing facilities, and other data collection elements have been finalized and are now complete.

<u>Task 2 (Month 3-12)</u> Subject recruitment logistics, data collection and data management for Studies 1-3 – COMPLETED

Subject recruitment, data collection and data management efforts have been completed for Studies 1-3. Recruitment of both Human Research Volunteers and Civilians was effective and efficient.

Task 3 (Month 15-24) Perform preliminary data analyses for Study 3– COMPLETED
All preliminary data analyses for Study 3 have been completed. Initial analyses suggested that additional participants would be necessary to explore noted differences between military and civilian participants on discrete on mood measures. Thus an amendment (#4, 14 July 2009) to increase enrollment from 50 to 80 participants was submitted and approved. Higher-level analyses are nearing completion on this expanded sample.

Task 4 (Month 15-24) Complete data collection for Study 1– COMPLETED
Study 1 involves the examination of common use practices and specific administration procedures (individual or group administration, practice or no practice, single session or two sessions) on ANAM4 task performances. Our recruitment goal for Study 1 was 90 participants, 30 participants per condition. This goal has been reached.

Table 2. Study 1 Enrollment

# Participants Enrolled	90
# Participants Completed	86*

**NOTE: 15 participants completed the ANAM4 without practice test modules; 15 participants completed the ANAM4 in a group setting and 15 participants completed the ANAM4 in two administration sessions. The remaining 41 participants served as controls for these discrete administration scenarios (individual administration using practice test modules and completed in a single testing session). Thus each condition had at least 30 participants, as required.*

Task 5 (Month 15-24) Perform preliminary data analyses for Study 1 – COMPLETED
Preliminary analyses (sample characterization and demographic analyses) on the Study 1 data set have been completed.

Task 6 (Months 15-24) Subject recruitment, data collection and data management for Studies 2 & 3 – COMPLETED
Our recruitment goal for Study 2 was 90 participants, 30 participants per condition (days 1 & 7 / days 1 & 30 / 7 consecutive day retest). Recruitment goal for Study 3 was 80 participants. Recruitment goals were reached for Studies 2 and 3 and data collection has been completed for these studies.

Task 7 (Months 15-24) Complete data collection for Study 3 – COMPLETED
Data collection for Study 3 is complete.

Table 3. Study 3 Enrollment

# Participants Enrolled	113
# Participants Completed	77

Task 8 (Months 25-36) Complete data collection for Study 2- COMPLETED
Data collection for Study 2 is complete.

Table 4. Study 2 Enrollment

# Participants Enrolled	99
# Participants Completed	92

<u>Task 9 (Months 25-36)</u> Plan and finalize logistics for Phase II (modified Study 4) – COMPLETE
The Study 4 protocol has been reviewed and approved by USARIEM HURC and HRPO (final approval to initiate received June 2011). Endorsement of the study by the National Guard Bureau was received 20 October 2011 and all 8 states (Arizona, Kentucky, Maine, Minnesota, Mississippi, Montana, Oklahoma, Pennsylvania) have been contacted by both NGB and study staff.

<u>Task 10 (Months 25-36)</u> Complete data analyses for Studies 1, 2, 3 - IN PROGRESS
Preliminary data analyses have been completed for each of the studies. We are currently conducting higher-level analyses for data within each of these studies.

<u>Task 11 (Months 25-36)</u> Preparation of journal manuscript(s) for Studies 1, 2, 3 – IN PROGRESS
Manuscripts for each of these studies are in draft form and are waiting for completion of higher-level analyses to finalize and submit to peer-reviewed journals.

<u>Task 12 (Months 25-36)</u> Preparation of project report for Studies 1, 2, 3 – COMPLETED
Project summaries and completion of Studies 1-3 were included in previous continuing review reports. Manuscripts for these studies are in progress.

<u>Task 13 (Months 25-36)</u> Set-up data management procedures for Study 4 - COMPLETED
All procedures involving data management have been established. Study datasets have been created and are being populated as data are obtained from field sites. Data entry and checking have been successfully coordinated.

<u>Task 14 (25-36)</u> Initiate data collection procedures for Study 4 – COMPLETED
We currently have TAG approvals from AZ and ME and are awaiting final TAG approvals from OK, MN, MT. Data collection was initiated in AZ in June 2011 and is currently ongoing. We have met with ME ARNG personnel and currently coordinating dates for data collection with them.

<u>Task 15 (37-48)</u> Carry out data collection procedures for Study 4 – IN PROGRESS
Data collection was initiated in AZ in June 2011 and is currently ongoing. We have met with ME ARNG personnel and currently coordinating dates for data collection with them.

<u>Task 16 (37-48)</u> Initiate integrative data management structure set up for Study 4 - COMPLETED
Databases associated with Study 4 data have been created and are being populated as data are obtained.

Task 17 (37-48) Operationalize database for Study 4 analysis scheme – IN PROGRESS
Data entry has commenced and databases continue to be refined for analytic schemes.

Task 18 (37-48) Perform preliminary data analyses for Study 4 - PENDING

Task 19 (49-60) Complete data collection procedures for Study 4 - PENDING

Task 20 (49-60) Complete data analyses for Study 4 – PENDING

Task 21 (49-60) Prepare Study 4 manuscript(s) for peer review – PENDING

Task 22 (49-60) Preparation of Project Final Report – PENDING

KEY RESEARCH ACCOMPLISHMENTS

Key research accomplishments during the current study period include:

- Recruitment and data collection have been completed for Studies 1, 2 and 3.
- Data analysis and manuscript preparation for Studies 1, 2 and 3 are in progress.
- Continuing Review report was reviewed and approved by the USARIEM HURC (30 March 2011).

REPORTABLE OUTCOMES

Reportable outcomes during the current study period include:

1. Reports, manuscripts, abstracts (Abstract is included in Appendix)

The following manuscript, submitted for publication, was supported, in part by this award (W81XWH-08-1-0021):
Maruta J, Heaton KJ, Kryskow EM, Maule, AL, Ghajar J. Assessment of dynamic predictive timing with indices of visuo-motor synchronization during circular ocular pursuit. Behavior Research Methods*, under review.*

2. Degrees and research training opportunities

Two graduate-level students, two master's-level students, and five undergraduate students have been trained to administer the study protocol for this project.

3. Collaborative funding applications related to work supported by this award

The following funded projects are directly related to the work supported by this award:

- "Eye-Tracking Rapid Attention Computation (EYE-TRAC)" (USARIEM Protocol # H09-07; Site PI: Heaton). This project was funded as a FY08 CDMRP Advanced Technology Award to Dr. Jamshid Ghajar, Brain Trauma Foundation, New York, NY

(W81XWH-08-2-0646). This project includes an ANAM4 task battery (ANAM 4 TBI Battery) as part of the protocol, with ANAM 4 data being collected at 4 time points, allowing for computation of test-retest reliability across a 2 week interval and sensitivity of the ANAM4 TBI battery to differentiate performance between a rested and fatigued (24 hour sleep deprivation) state. This project is ongoing.

- "An Investigation of the Effects of Head Impacts Sustained during Collegiate Boxing Participation on Central and Peripheral Nervous System Function" (USAFA Protocol # FAC2007010H, PI: MAJ Brandon Doan, USAFA), was funded in part by an AMEDD Advanced Medical Technology Initiative (AAMTI) award to Dr. Heaton and includes use of the ANAM4. Data collection is complete; manuscripts are in progress.

- "Validation of Select Neurobehavioral Assessments for Concussion/Mild Traumatic Brain Injury (MTBI)" (USARIEM #H09-08), was intramurally funded (MRMC RAD3) to Drs. Proctor and Heaton (co-PIs). This study seeks to validate the ANAM4TBI Battery against a standard neuropsychological screening battery for mild traumatic brain injury. The project is ongoing.

- "Identifying biomarkers that distinguish post-traumatic stress disorder and mild traumatic brain injury using advanced magnetic resonance spectroscopy," was funded via a Department of Defense Congressionally Directed Medical Research Programs Psychological Health/Traumatic Brain Injury (PH/TBI) Research Program award to Dr. Alex Lin, Brigham and Women's Hospital, Boston, MA. Dr. Heaton is a co-Investigator and site PI on this project. This study proposes a multi-parametric approach using major advances on spectroscopic methods and neuroimaging to identify biomarkers that can be used to distinguish between post-traumatic stress disorder, traumatic brain injury, and their co-occurrence. This will be achieved in part by correlating quantitative MR spectroscopy results with behavioral and neuropsychological metrics (including ANAM4) using newly developed algorithmic approaches that are capable of revealing discriminating metabolic markers in MR spectroscopy measurements. The funding period for this project is 11/10-10/13; the protocol is currently under IRB review.

4. Related projects and collaborations initiated

- "Microclimate cooling for air soldier flight crew" (USARIEM Protocol 11-08-H) (PI: Mr. Bruce Cadarette, USARIEM; Research Associate: Dr. Heaton)
- "Analyses of ANAM4 TBI predeployment assessment data: USARIEM-OTSG research collaborative" (USARIEM Protocol 11-07-HC) (PI: Dr. Proctor; Co-I: Dr. Heaton)
- "Identifying biomarkers that distinguish post-traumatic stress disorder and mild traumatic brain injury using advanced magnetic resonance spectroscopy," (2007-P-002458/9; Brigham and Women's Hospital) Department of Defense U.S. Army Medical Research and Material Command Congressionally Directed Medical Research Programs, 2009 Psychological Health and Traumatic Brain Injury Research Program Award (PI: Dr. Alexander Lin, Brigham and Women's Hospital; Co-I: Dr. Heaton)

- "Noninvasive Cerebral Glutamate Monitoring in Veterans with Traumatic Brain Injury" Harvard Catalyst Pilot Grant, (PI: Dr. Alexander Lin, Brigham and Women's Hospital; Co-I: Dr. Heaton)
- Massachusetts Institute of Technology Lincoln Laboratories: collaborations with Dr. Heaton aimed at developing multi-modal assessments for mild TBI/concussion (with Jonathan Su, Ph.D., Laurel Reilly-Raska, Ph.D.), and validation of novel biophysiologic measures of fatigue, brain injury, and stress (with Tom Quatieri, Ph.D., Nick Malyska, Ph.D.).

CONCLUSIONS

There has been steady, and significant, progress in this current funding period. Data from Studies 1-3 are being analyzed and manuscripts are being prepared in preparation for submission to peer-reviewed journals. Study 4 has been approved by both USARIEM HURC and HRPO. National Guard Bureau has provided endorsement of the study and all eight identified states have been contacted. Data collection has commenced in AZ and is being coordinated in ME. We have received positive responses from three additional states (MN, MT, OK) and are awaiting TAG approvals.

Data from this project will contribute to ongoing efforts to validate the ANAM4 and inform use of this assessment tool and interpretation of testing results within a military population.

APPENDIX

Maruta J, Heaton KJ, Kryskow EM, Maule, AL, Ghajar J. Assessment of dynamic predictive timing with indices of visuo-motor synchronization during circular ocular pursuit. Behavior Research Methods, *under review.*

Abstract

When visually tracking a moving target, spatial and temporal predictions are used to circumvent the neural delay required for the visuo-motor processing. However, the internally generated predictions must be synchronized to the external stimulus during continuous tracking. We examined the utility of a circular visual tracking paradigm for assessment of predictive timing using normal human subjects. Disruptions of gaze-target synchronization were associated with anticipatory saccades that caused the gaze to be temporarily ahead of the target along the circular trajectory. These anticipatory saccades indicated preserved spatial and temporal prediction but suggested that the timing of the execution of the temporal prediction, i.e. predictive timing, was impaired. We quantified gaze-target synchronization with several indices, whose distributions across subjects were such that instances of extremely poor performances were identifiable outside the margin of error determined by test-retest measures. Because predictive timing is an important element of attention functioning, the visual tracking paradigm and indices described here may be useful for attention assessment.

Key words: attention; smooth pursuit; test-retest reliability; concussion; traumatic brain injury